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Regeneration Roadmap

University of Dayton, Ohio (url: http://www.udayton.edu/index.php)

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Scientists at the University of Dayton have mapped out the process at the genetic level newts use to regenerate lenses, limbs and other tissue.

The research, published this week in BioMed Central's open access journal *Genome Biology*, identifies the protein families expressed during tissue regeneration in the common North American newt, laying the groundwork for research into what particular sets of genes are used for this purpose. This is the first comprehensive map of all RNA molecules — called the transcriptome — expressed in regeneration.

"This is the first time the newt transcriptome has been constructed, especially in relation to regeneration," said Panagiotis Tsonis, a co-author of the study. "Several new protein families have been identified and this could provide unprecedented insights to regeneration processes and as to why other animals do not have the abilities of the newts."

Newt and salamander genomes are enormous — currently too big to sequence. But the vertebrates' potential to regenerate entire limbs, along with parts of the central nervous system, has fascinated scientists for more than 200 years.

Tsonis, director of the University of Dayton's Center for Tissue Regeneration and Engineering at Dayton (TREND), Thomas Braun and Thilo Borchardt at the Max Planck Institutes in Germany and their colleagues sequenced a collection of healthy and regenerated tissues from newts, and converged them into one comprehensive transcriptome. Their analysis identified 826 proteins specific to the salamander family and several newly identified proteins they believe may play important roles in the regeneration process unique to this family of amphibians. Their data also outline genes that appear only in regeneration but not uninjured material, which will be of interest in regenerative medicine.

The transcriptome is not complete, but it serves as a foundation for further analyses. The authors believe their findings represent only the start and can lay the groundwork for experiments to determine if salamanders use genes unique to them for tissue regeneration.

Tsonis has studied tissue regeneration in the newt for more than 32 years and is currently working with a five-year, $1.8 million grant to continue his study of lens regeneration in the newt and its connection to stem cell research. The grant, awarded in 2009, is the sixth and largest grant Tsonis has received from the National Institutes of Health, which has funded his research continuously since 1995. In all, he's received nearly $7 million in research funding from the NIH, the Arthritis Foundation and others.

He has become a leading voice in regeneration research. In 2011, he published groundbreaking work in *Nature Communications* that overturned 250 years of scientific theory regarding regeneration. In a study spanning 16 years, he concluded old age and repeated regeneration do not alter the capacity of newts to regenerate tissue. The 17th lens was just as perfect as the first new lens.

Eight years ago, he and his wife Katia Del Rio-Tsonis, a biologist at Miami University, succeeded in causing tissue to regenerate where it never had before. In a newt's eye, the upper iris can regenerate a lens after injury, but the lower iris cannot. By adding the right mix of certain growth factors – sort of like a recipe – they were finally able to induce the lower iris to grow a new lens. *Nature* published the findings in 2005.

The TREND Center at the University of Dayton is an Ohio Center of Excellence in the field of biomedicine and health care and includes a research alliance with Wright State University, the Kettering Medical Center Network, Rice University and other universities. Established in 2006, it has more than 20 researchers participating from six academic departments and the University of Dayton Research Institute. Center investigators maintain nearly $5 million in research contracts and grants, and have compiled more than 500 peer-reviewed articles.

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